ANALYSIS

SCIENCE AND MEDICINE

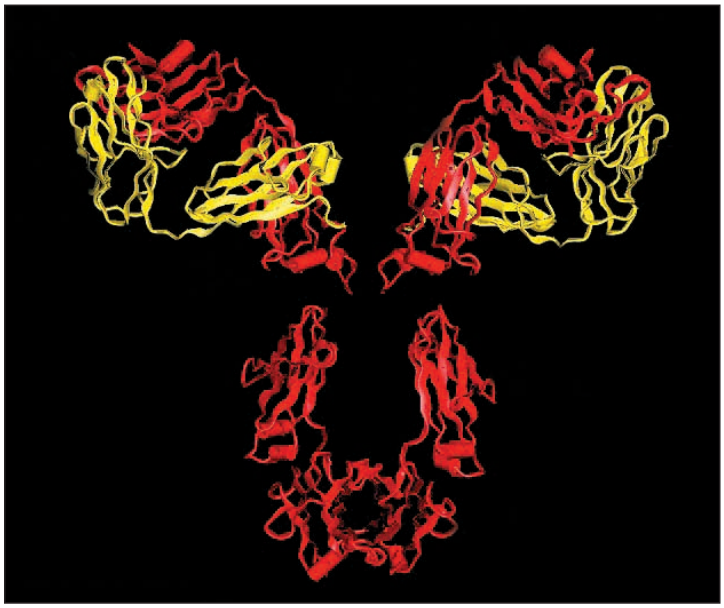
Immunotherapy made more accessible?

Monoclonal antibodies have been developed for the treatment of numerous diseases, but their manufacture is lengthy and labour intensive. A recent discovery may lead to improved production, however. In a new study, Fang and colleagues demonstrate that it is possible to transfer genes that encode for monoclonal antibody into an animal, allowing the expression of a biologically active monoclonal antibody in vivo.[1]

Antibodies are manufactured for a variety of uses. Immunosuppressive monoclonal antibodies have been created to prevent rejection of transplanted organs. Daclizumab, for example, binds to an interleukin receptor on T-cells, thus preventing lymphocyte activation. Other antibodies target infectious agents to inhibit their replication: palivizumab has been shown to decrease hospital admission rates among children with respiratory syncitial virus infection. The high cost of treatment, however, has limited its use to children with comorbidities and a high risk of complications.

An alternative strategy to manufacturing monoclonal antibodies is inducing the body to produce the antibodies itself.[2] This has proved difficult, since antibody genes are typically too large to be transported in vectors that would facilitate their easy expression (usually viruses). To date, many attempts to achieve therapeutic serum levels of monoclonal antibodies have failed.[1]

Fang and colleagues recently developed a method to repackage the DNA of a gene encoding a monoclonal antibody with known antiangiogenic effects in mouse tumour models. The sequences that code for the 2 portions of the antibody — known as heavy and light chains — were inserted into a viral vector beside a sequence that codes for a peptide derived from the foot-and-mouth disease virus. The peptide sequence acted as a bridge, enabling the sequences for the heavy and light chains to be read together. With this technique, antibody production was induced in mice with no apparent deleterious effects. Furthermore, after cancer cells were introduced into these mice, the researchers determined that the antibody was indeed biologically active since the mice lived longer and exhibited longer tumour dormancy than control mice.



This representation of a model of a human immunoglobulin IgG1 antibody shows the 2 heavy chains in red and the 2 light chains in yellow. Reproduced with the permission of Dr. Mike Clark, Cambridge University.

New and improved delivery systems are an important focus of research, given the therapeutic promise of monoclonal antibodies. Although inducing the body to produce antibodies will require ways to control antibody levels and autoimmune reaction,[2] the delivery system discovered by Fang and colleagues is a step in the right direction. — *David Secko*, Vancouver

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References

1. Fang J, Qian JJ, Yi S, Harding TC, Tu GH, VanRoey M, et al. Stable antibody expression at therapeutic levels using the 2A peptide. *Nat Biotech* 2005;23(5):584-90.
2. Bakker JM, Bleeker WK, Parren PW. Therapeutic antibody gene transfer: an active approach to passive immunity. *Mol Ther* 2004;10(3):411-6.